UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/512,701	02/25/00	LEONARD J	GI5229FWC-DI

025291 HM12/0828
AMERICAN HOME PRODUCTS CORPORATION
PATENT SECTION
FIVE GIRALDA FARMS
MADISON NJ 07940-0874

EXAMINER	
MINNIFIELD,N	
ART UNIT	PAPER NUMBER
1645	9

DATE MAILED: 08/28/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/512,701	LEONARD ET AL.	
	Examiner	Art Unit	
	Nita M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *15 June 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

1. Applicants' amendment filed June 15, 2001 is acknowledged and has been entered. Claims 17-20 have been amended. Claims 16-20 are now pending in the present application. All rejections have been withdrawn in view of Applicants' amendment with the exception of those discussed below.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 16-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to a method for treating rheumatoid arthritis in a human subject comprising administering to the subject IL-12 antagonist (antibody or antibody fragment immunoreactive with IL-12).

The specification teaches that interferon-gamma is implicated in the development, exacerbation and/or recurrence of numerous autoimmune conditions, and that interferon-gamma is associated the multiple sclerosis, IDDM and rheumatoid arthritis. The examples set forth in the specification teach EAE in mice as a useful model for multiple sclerosis (p. 14). In vitro experiments are set forth on page 15. In vivo administration of IL-12 or IL-12 antagonist are set forth on pages 16 and 20. In vitro data on the effects of IL-12 on interferon-gamma are set forth on page 18. In vivo data on the effects of IL-12 with regard to IDDM are set forth on page 21.

However, the specification does not set forth any guidance, evidence or examples with regard to a method for treating rheumatoid arthritis in a human subject comprising administering to the subject IL-12 antagonist (antibody or antibody fragment immunoreactive with IL-12). The specification does not enable one of ordinary skill in the art to practice the claimed invention. Furthermore, the art teaches that anti-IL-12 has no statistically significant effect on the clinical outcome of disease, arthritis (abstract; p. 2206, Butler et al, 1999). Butler et al teach that the actions of both antibodies (anti-IL-12 and anti-TNF) were synergistic and that anti-IL-12 alone had little effect on clinical disease (p. 2209). "We have previously described that anti-IL-12 can prevent development of the Th1 response towards CII thus reducing arthritis, when administered from immunization onwards. We have now found that after the onset of disease, treatment with anti-IL-12, on its own, was not capable of skewing the Th1 response to CII and lacked therapeutic effect..." (p. 2209, col. 2). In view of the teachings in the art and the lack of guidance, evidence or examples in the specification with regard to a method for treating rheumatoid arthritis in a human subject comprising administering to the subject IL-12 antagonist (antibody or antibody fragment immunoreactive with IL-12), claimed invention the claimed invention is not enabled.

The rejection is maintained for the reasons of record. Applicant's arguments filed June 15, 2001 have been fully considered but they are not persuasive. Applicants have argued that the specification sets forth dosage regimens and how to use antagonists against IL-12 in the treatment of autoimmune diseases such as rheumatoid arthritis (specification, pp. 2, 4, 6). However, the specification does not teach a method for treating rheumatoid arthritis in a human subject comprising administering to the subject IL-12 antagonist (antibody or antibody fragment immunoreactive with IL-12). The specification does not enable one of ordinary skill in the art to practice the claimed invention. With regard to Applicants' arguments that Butler et al cannot establish that

the claimed method would not work in treatment of human patients, the art of Butler et al teaches that anti-IL-12 has no statistically significant effect on the clinical outcome of disease, arthritis (abstract; p. 2206, Butler et al, 1999). Butler et al teach that the actions of both antibodies (anti-IL-12 and anti-TNF) were synergistic and that anti-IL-12 alone had little effect on clinical disease (p. 2209). "We have previously described that anti-IL-12 can prevent development of the Th1 response towards CII thus reducing arthritis, when administered from immunization onwards. We have now found that after the onset of disease, treatment with anti-IL-12, on its own, was not capable of skewing the Th1 response to CII and lacked therapeutic effect..." (p. 2209, col. 2). The sample size is not relevant with regard to the presently claimed invention. The specification has not shown that even an animal model for rheumatoid arthritis could be treated with antagonist against IL-12. It is noted that Applicants cited two other references with regard to the role of IL-12 in rheumatoid arthritis, however each of these references were filed after the filing date of the claimed invention. Further, the inventive entity of the claimed invention and the authors of these references are different. It is not clear that Applicants are the inventors or reduced the invention to practice. The specification is only enabled for treatment of MS using antagonists against IL-12. Any evidence to the contrary, regarding the enablement of the claimed invention of a method for treating rheumatoid arthritis in a human subject comprising administering to the subject IL-12 antagonist (antibody or antibody fragment immunoreactive with IL-12) will be considered by the Examiner.

4. No claims are allowed.

5. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nita M. Minnifield whose telephone number is 703-305-3394. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 703-308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Nita M. Minnifield
Primary Examiner
Art Unit 1645

August 23, 2001